CLAIMS

1. A pharmaceutical composition for therapeutic or prophylactic administration to a subject having an infective disease or at risk for contracting an infective disease, the composition comprising an aqueous carrier having in solution therein (a) a benzoquinolizine-2-carboxylic acid antimicrobial drug or salt, polymorphic form, enantiomeric form, other isomeric or racemic form thereof in a therapeutically or prophylactically effective drug concentration that is above the practical limit of solubility of the drug in a substantially isotonic aqueous solution at a physiologically compatible pH, and (b) a pharmaceutically acceptable solubilising agent selected from a basic amino-acid, a cyclodextrin, a cyclodextrin polymer or derivative theref or a mixture thereof in a concentration sufficient to maintain the drug in solution at drug concentration that is above the practical limit of solubility of the drug in a substantially isotonic aqueous solution at a physiologically compatible pH.

2. The composition of claim 1, that is suitable for parenteral administration.

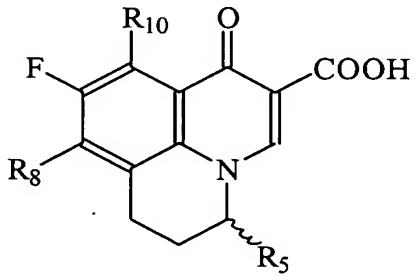
3. The composition of claim 1, that is suitable for intravenous injection or infusion.

4. The composition of claim 1, wherein the concentration of a drug is about 1 mg/ml to about 100 mg/ml.

5. The composition of claim 1, wherein the concentration of a drug is about 4 mg/ml to about 12 mg/ml.

6. The composition of claim 1, wherein the concentration of a drug is about 5 mg/ml to about 9 mg/ml.

7. The composition of claim 1, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug is selected from a compound of the formula:



(II)

wherein:

R_5 is C_{1-6} alkyl, as a mixture of enantiomers or in a stereochemical orientation;

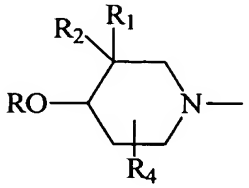
R_8 is 4-hydroxypiperidinyl optionally further substituted with one or more C_{1-6} alkyl, hydroxypiperidinyl optionally further mono/poly substituted with C_{1-6} alkyl;

R_{10} is selected from H, C_{1-5} alkyl, amino, alkylamino or acylamino group; or an optical isomer, diastereomer or enantiomer thereof, or a polymorph, pseudopolymorph or a prodrug thereof or pharmaceutically acceptable salt or hydrate thereof or a mixture thereof.

8. The composition of claim 7 wherein in the formula (I),

R_5 is CH_3, in S-orientation.

R_8 is



wherein:

R is hydrogen, C_1-C_6 alkyl, glycosyl, aralkyl , C_1-C_6 alkanoyl , or aminoalkanoyl or R is $C_6H_{11}O_6$, PO_3H_2 or SO_3H thus giving respectively the gluconic acid, phosphoric acid and sulfonic acid ester derivatives of the compounds;

R_1 and R_2 are the same or different and are selected from H, C_{1-4} alkyl, aralkyl, aminoalkyl, trifluoroalkyl or halogen;

R_4 is H, C_{1-4} alkyl, CF_3, phenyl, or F; R_4 is present at one or more of the positions of 2-, 4-, 5-, or 6- of the piperidine ring; and

R_{10} is selected from H, C_{1-5} alkyl, amino, alkylamino or acylamino groups.

9. The composition of claim 7, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug is selected from the group consisting of:

RS-(±)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo [i,j]quinolizine-2-carboxylic acid;

R(+)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo [i,j]quinolizine-2-carboxylic acid;

S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo [i,j]quinolizine-2-carboxylic acid;

RS-(±)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo [i,j]quinolizine-2-carboxylic acid arginine salt and solvatomorphic or polymorphic forms thereof;

R(+)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo [i,j]quinolizine-2-carboxylic acid arginine salt and solvatomorphic or polymorphic forms thereof;

S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo [i,j]quinolizine-2-carboxylic acid arginine salt and solvatomorphic or polymorphic forms thereof;

RS-(±)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo [i,j]quinolizine-2-carboxylic acid 0.2 hydrate;

R(+)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo [i,j]quinolizine-2-carboxylic acid 0.2 hydrate;

S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo [i,j]quinolizine-2-carboxylic acid 0.2 hydrate;

S-(-)-9-fluoro-6,7-dihydro-8-{trans-4-(RS)-hydroxy-3-(RS)-methylpiperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid;

S-(-)-9-fluoro-6,7-dihydro-8-{cis-4-(RS)-hydroxy-3-(RS)-methylpiperidin-1-yl-5-methyl-oxo-1H,5H-benzo[i, j]quinolizine-2-carboxylic acid;

S-(-)-9-fluoro-6,7-dihydro-8-{cis-(-)-4-R-hydroxy-3-S-methylpiperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i, j]quinolizine-2-carboxylic acid;

S-(-)-9-fluoro-6,7-dihydro-8-{cis-(+)-4-S-hydroxy-3-R-methylpiperidin-1-yl}-5-methyl-1-oxo-1H,5H-benzo[i, j]quinolizine-2-carboxylic acid; and

S-(-)-9-fluoro-6,7-dihydro-8-(3-ethyl-4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid (mixture of cis racemate and trans racemate) and pure stereoisomers thereof.

10. The composition of claim 9, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug is S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid arginine salt, or a solvatomorphic or polymorphic form thereof.

11. The composition of claim 9, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug is S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid 0.2 hydrate.

12. The composition of claim 9, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug is S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid.

13. The composition of claim 1, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug comprises about 0.1% to about 1.0 % by weight of the composition.

14. The composition of claim 1, wherein the amino acid is selected from arginine, histidine, arginine acetate, arginine-glutamate, arginine monohydrochloride, histidine acetate, histidine acetate dihydrate, histidine monohydrochloride, histidine monohydrochloride monohydrate, lysine, lysine acetate, lysine monohydrochloride, ornithine, tryptophan or salts thereof.

15. The composition of claim 14, wherein the amino acid comprises L-arginine.

16. The composition of claim 14, wherein the amino acid comprises L-lysine.

17. The composition of claim 1, wherein the cyclodextrin polymer is selected from α-cyclodextrin, β-cyclodextrin, γ-cyclodextrin, hydroxypropyl β-cyclodextrin or derivatives thereof.

18. The composition of claim 17, wherein the cyclodextrin polymer comprises hydroxypropyl β-cyclodextrin.

19. The composition of claim 1, wherein the solubilizing agent comprises about 1.5 % to about 3.5 % by weight of the composition.

20. The composition of claim 14, wherein the solubilizing agent is amino acid and comprises about 0.1 % to about 1.4 % by weight of the composition.

21. The composition of claim 17, wherein the solubilizing agent is cyclodextrin polymer and comprises about 1.5 % to about 3.5 % by weight of the composition.

22. The composition of claim 1, further comprising a pharmaceutically acceptable vehicle comprising a modifying agent selected from acids, bases, inorganic basic salts, organic basic salts, buffering agents or mixtures thereof and/or an agent for adjusting osmolality in amounts whereby the solution is substantially isotonic and has a physiologically acceptable pH.

23. The composition of claim 1, that is in a physical form selected from a concentrate, lyophilisate, powder, solution, or suspension.

24. A method of treating and/or preventing a bacterial infection disease in a subject comprising administering to the subject, a pharmaceutical composition of claim 1 in a therapeutically or prophylactically effective dose.

25. The method of claim 24, wherein the composition is diluted in a pharmaceutically acceptable liquid prior to being administered to the subject.

26. The method of claim 24, wherein the subject is a human or animal subject.

27. The method of claim 24, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug is selected from S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid arginine salt, or solvatomorphic or polymorphic forms thereof;

S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid 0.2 hydrate; or

S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid.

28. The method of claim 24, wherein the daily dose is about 0.01 mg to 100 mg/kg of S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid, its arginine salt or 0.2 hydrate thereof.

29. The method of claim 24, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug comprises about 0.1 to 10% by weight of the composition.

30. The method of claim 24, wherein said solubilizing agent is selected from the group consisting of amino acids, cyclodextrin polymers or their derivatives, or mixtures thereof.

31. The method of claim 24, wherein said composition is administered by intravenous injection or infusion.

32. The method of claim 24, wherein the route of administration is parenteral.

33. A process for preparing a pharmaceutical composition comprising: mixing a pharmaceutically effective amount of benzoquinolizine-2-carboxylic acid antimicrobial drug of the formula (I) according to claim 1 with a pharmaceutically acceptable vehicle comprising a solubilizing agent at a concentration effective to maintain the drug in solution at physiologically compatible pH.

34. The process of claim 33, wherein said solubilizing agent is selected from amino acids, cyclodextrin polymers or their derivatives, or mixtures thereof.

35. The process of claim 34, wherein the benzoquinolizine-2-carboxylic acid antimicrobial drug is S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid arginine salt, solvatomorphic or polymorphic forms thereof; S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid 0.2 hydrate, or S-(-)-9-

fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid.